AMENDMENT

In the claims:

Please cancel claim 2 without prejudice and without disclaimer.

Please amend the claims as follows:

1. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence drawn from the group consisting of SEQ ID NO:3 and SEQ ID NO:5.

2. (Cancelled)

3. (Cancelled)

4. (Original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:6.

5. (Previously Presented) The isolated nucleic acid molecule of claim 4, comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.

6. (Previously Presented) The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO:3.

7. (Previously Presented) The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO:5.

8. (Previously Presented) A recombinant expression vector comprising a nucleic acid molecule that encodes the amino acid sequence shown in SEQ ID NO:6.

9. (Previously Presented) The recombinant expression vector of claim 8, wherein said nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:5.

10. (Previously Presented) The recombinant expression vector of claim 8, wherein said nucleic

acid molecule encodes the amino acid sequence shown in SEQ ID NO:4.

11. (Previously Presented) The recombinant expression vector of claim 10, wherein said nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:3.

12. (Previously Presented) A host cell comprising the recombinant expression vector of claim 8.

13. (New) The host cell of claim 12, wherein said recombinant expression vector comprises a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:5.

14. (New) The host cell of claim 12, wherein said recombinant expression vector comprises a nucleic acid molecule encoding the amino acid sequence shown in SEQ ID NO:4.

15. (New) The host cell of claim 14, wherein said recombinant expression vector comprises a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:3.

RESPONSE

I. Status of the Claims

Claim 2 has been cancelled without prejudice and without disclaimer. No claims have been amended. New claims 13-15 have been added.

Claims 1 and 4-15 are therefore presently pending in the case.

II. Support for the Newly Added Claims

Claims 13-15 have been added to specifically recite alternative embodiments of claim 12. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 14, lines 23-29.

It will be understood that no new matter is included within the newly added claims.

III. Rejection of Claims 1, 2 and 4-12 Under 35 U.S.C. § 101

The Action first rejects claims 1, 2 and 4-12 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that claim 2 lacks a patentable utility, as claim 2 has been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claim 2 under 35 U.S.C. § 101 is rendered moot. The remainder of this section will therefore focus on claims 1 and 4-12.

In the specification as originally filed, Applicants assert that the presently claimed sequences "share structural similarity with mammalian membrane proteins such as cell adhesion proteins" (specification at page 2, lines 2-3). Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55; **Exhibit A**) clearly establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility (see Section IV, below), is not proper when a full length sequence (such as the presently claimed sequence) has a similarity score greater than 95% to a protein having a "well established utility". Applicants respectfully point out that the presently claimed nucleotide sequences and encoded amino acid sequences shares nearly **100% identity** over the entire length of the coding sequence with a nucleotide sequence and the encoded amino acid

sequence that are described and claimed in a recently issued U.S. Patent (U.S. Patent No. 6,656,707, issued December 2, 2003, nucleotide sequence SEQ ID NO:1 and amino acid sequence SEQ ID NO:2; **Exhibit B**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). The nucleic acid alignment between SEQ ID NO:3 and the patented nucleic acid sequence ("Query"; as presented in GenBank accession number AR435509) is provided in **Exhibit C**, and the amino acid alignment between SEQ ID NO:4 ("SEQ") and the patented amino acid sequence ("gi|401"; as presented in GenBank accession number AAR79125.1) is provided in **Exhibit D**. As the United States Patent and Trademark Office has clearly established that the sequence claimed in U.S. Patent No. 6,656,707 has a patentable utility, there can be no question that Applicants' sequence, which shares almost **100% identity** with the patented sequence, must also have a patentable utility. Therefore, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

It has been well established that Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), and, thus, any questions concerning whether or not the present claims meet the requirements of 35 U.S.C. § 101 should have been laid to rest. Nevertheless, the present invention has a number of additional substantial and credible utilities, not the least of which is in forensic biology, as described in the specification, at least at page 3, line 12. As described in the specification from page 17, line 1 to page 19, line 16, the present sequence defines a number of single coding single nucleotide polymorphisms, specifically: a G/A polymorphism at nucleotide position 1,102 (of SEQ ID NOS:3 and 5) that can result in either an alanine or threonine being present at corresponding amino acid (aa) position 368 (of SEQ ID NOS:4 and 6); a silent A/C polymorphism at nucleotide position 1,306 (of SEQ ID NOS:3 and 5), both of which result in an arginine being present at corresponding aa position 436 (of SEQ ID NOS:4 and 6); a C/T polymorphism at nucleotide position 1,823 (of SEQ ID NOS:3 and 5) that can result in either an alanine or valine being present at corresponding aa position 608 (of SEQ ID NOS:4 and 6); an A/C polymorphism at nucleotide position 2,143 (of SEQ ID NOS:3 and 5) that can result in either a threonine or proline being present at corresponding aa position 715 (of SEQ ID NOS:4 and 6); a silent A/C polymorphism at nucleotide position 2,202 (of SEQ ID NOS:3 and 5), both of which result in a valine being present at corresponding aa position 734 (of SEQ ID NOS:4 and 6); a silent A/G

polymorphism at nucleotide position 2,283 (of SEQ ID NOS:3 and 5), both of which result in a glutamate being present at corresponding aa position 761 (of SEQ ID NOS:4 and 6); a G/A polymorphism at nucleotide position 2,285 (of SEQ ID NOS:3 and 5) that can result in either a glycine or glutamate being present at corresponding aa position 762 (of SEQ ID NOS:4 and 6); a silent A/C polymorphism at nucleotide position 2,601 (of SEQ ID NOS:3 and 5), both of which result in a glycine being present at corresponding aa position 867 (of SEQ ID NOS:4 and 6); an A/G polymorphism at nucleotide position 2,696 (of SEQ ID NOS:3 and 5) that can result in either a lysine or arginine being present at corresponding aa position 899 (of SEQ ID NOS:4 and 6); an AG/TT polymorphism at nucleotide positions 2,776-2,777 (of SEQ ID NOS:3 and 5) that can result in either a leucine or arginine being present at corresponding aa position 926 (of SEQ ID NOS:4 and 6); an A/C polymorphism at nucleotide position 2,873 (of SEQ ID NOS:3 and 5), which results in either an asparagine or threonine being present at corresponding aa position 958 (of SEQ ID NOS:4 and 6); a silent G/A polymorphism at nucleotide position 3,114 (of SEQ ID NOS:3 and 5), both of which result in a glycine being present at corresponding aa position 1038 (of SEQ ID NOS:4 and 6); an AT/TC polymorphism at nucleotide positions 3,115-3,116 (of SEQ ID NOS:3 and 5) that can result in either a methionine or serine being present at corresponding aa position 1,039 (of SEQ ID NOS:4 and 6); a C/A polymorphism at nucleotide position 4,246 (of SEQ ID NOS:3 and 5), which results in either a glutamine or lysine being present at corresponding aa position 1,416 (of SEQ ID NOS:4 and 6); a G/A polymorphism at nucleotide position 4,813 (of SEQ ID NOS:3 and 5), which results in either a valine or methionine being present at corresponding aa position 1,605 (of SEQ ID NOS:4 and 6); a C/A polymorphism at nucleotide position 5,429 (of SEQ ID NOS:3 and 5), which results in either an alanine or glutamate being present at corresponding aa position 1,810 (of SEQ ID NOS:4 and 6); an A/T polymorphism at nucleotide position 5,527 (of SEQ ID NOS:3 and 5), which results in either a lysine or STOP being present at corresponding aa position 1,843 (of SEQ ID NOS:4 and 6); a C/T polymorphism at nucleotide position 6,089 (of SEQ ID NO:3), which results in either an alanine or valine being present at corresponding aa position 2,030 (of SEQ ID NO:4); a C/G polymorphism at nucleotide position 6,092 (of SEQ ID NO:3), which results in either a serine or cysteine being present at corresponding aa position 2,031 (of SEQ ID NO:4); a C/G polymorphism at nucleotide position 6,094 (of SEQ ID NO:3), which results in either a proline or alanine being present at corresponding aa position 2,032 (of SEQ ID NO:4); an AC/CT polymorphism at nucleotide positions 7,868-7,869 (of SEQ ID NO:3), which results in either an aspartate or alanine being present at corresponding aa

position 2,623 (of SEQ ID NO:4); a silent A/G polymorphism at nucleotide position 8,250 (of SEQ ID NO:3), both of which result in an alanine being present at corresponding aa position 2,750 (of SEQ ID NO:4); a silent T/C polymorphism at nucleotide position 8,754 (of SEQ ID NO:3), both of which result in a histidine being present at corresponding aa position 2,918 (of SEQ ID NO:4); a C/A polymorphism at nucleotide position 9,170 (of SEQ ID NO:3), which results in either a proline or histidine being present at corresponding aa position 3,057 (of SEQ ID NO:4); a G/T polymorphism at nucleotide position 9,176 (of SEQ ID NO:3), which results in either a cysteine or phenylalanine being present at corresponding aa position 3,059 (of SEQ ID NO:4); a T/A polymorphism at nucleotide position 9,481 (of SEQ ID NO:3), which results in either a phenylalanine or isoleucine being present at corresponding aa position 3,161 (of SEQ ID NO:4); a silent T/A polymorphism at nucleotide position 9,576 (of SEQ ID NO:3), both of which result in a valine being present at corresponding aa position 3,192 (of SEQ ID NO:4); and a G/A polymorphism at nucleotide position 9,625 (of SEQ ID NO:3), which results in either a glutamate or lysine being present at corresponding aa position 3,209 (of SEQ ID NO:4). As such polymorphisms are the basis for forensic analysis, which is undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner states that this utility is not specific and substantial because "the nucleic acids are not disclosed as indicative, prognostic or diagnostic to any particular condition" (the Action at page 3). Applicants first point out that the association of a particular disease with the claimed sequence is not the standard required for utility under 35 U.S.C. § 101 (*In re Brana,* 34 USPQ2d 1436 (Fed. Cir. 1995); "*Brana*"). In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption" (*Brana* at 1442). Additionally, Applicants respectfully point out that the use of the presently described polymorphisms in **forensic** analysis does **not** require the identification of a specific medical condition. The presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to distinguish individual members of the human population based on the presence or absence of one or both of the described polymorphisms. This is also not a case of a "potential" utility. Using the polymorphic markers exactly as described in the specification as originally field can definitely distinguish members of a population from one another. In the worst case scenario, each marker is useful to distinguish 50% of the population (in other words, a marker being

present in half of the population). Applicants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Applicants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). The ability to eliminate at least 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic marker is only potentially useful would be without merit, and would not support the alleged lack of utility.

The Examiner then states that such a use does not have a "'real world' significance" (the Action at page 4). Applicants hardly know where to begin. Naturally occurring genetic polymorphisms such as those described in the Sequence Listing are both the basis of, and critical to, *inter alia*, forensic genetic analysis intended to resolve issues of, for example, identity or paternity. Forensic analysis based on identified polymorphisms such as those identified by Applicants is used to positively identify or rule out suspects in many criminal cases, and in identifying human remains. Paternity determination is based on identified polymorphisms such as those identified by Applicants to positively identify or rule out individuals suspected of fathering a particular child. Therefore, Applicants find the Examiner's position particularly difficult to comprehend. What could be possibly be more substantial and real world than the loss of an individual's freedom or life through incarceration? What could be possibly be more substantial and real world than the positive identification of human remains? What could be possibly be more substantial and real world than the impact, both economic and emotional, that the results of a paternity analysis has on the individuals directly and indirectly involved? These are all well known and generally accepted uses of identified polymorphisms such as the polymorphisms identified by Applicants. Without such identified polymorphisms, the skilled artisan would not be able to carry out such forensic or paternal analyses. Thus, the Examiner's argument in **no way** supports the allegation that the presently claimed sequence lacks a patentable utility.

The Examiner also states that such a use is not specific or substantial because it is applicable to "any nucleic acid" (the Action at page 3). Applicants point out that not all nucleic acids contain polymorphic markers. In fact, the basis for forensic analysis is the fact that such polymorphic markers are not present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic

acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is meaningless. Additionally, the Examiner seems to be confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Following directly from the quote above, an invention does not need to be the best or only way to accomplish a certain result. Thus, the question of whether or not other nucleic acid sequences contain polymorphic markers is completely irrelevant to the present utility inquiry. The only relevant question in regard to meeting the standards of 35 U.S.C. § 101 is whether **every** nucleic acid can be so used - and the clear answer to this question is an emphatic **no**. Just because other, or even more useful, polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer, just to name a few particular examples, because the utility of each of these compositions is applicable to the broad class in which each of these compositions falls: all batteries have the same utility, specifically to provide electrical power; all automobile tires have the same utility, specifically for use on automobiles; all golf balls and golf clubs have the same utility, specifically for use in the game of golf; and all cancer treatments have the same utility, specifically, to treat cancer. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions nearly every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner then states that "(t)he recited uses also do not constitute a well-established utility

because the utility of the sequence is not established within the art" (the Action at page 4). As detailed above, the use of polymorphisms such as those described by Applicants are used by skilled artisans in forensic analysis **every day**, thus directly refuting the Examiner's argument that the use of polymorphisms in forensic analysis "is not established within the art". Furthermore, as the presently described polymorphisms are a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. Thus, the present claims meet the requirements of 35 U.S.C. § 101.

The Examiner further questions this asserted utility, stating that "further experimentation" would be required "to discover the 'real-world' significance or use of the nucleic acids claimed" (the Action at page 4). As set forth above, the present polymorphisms are useful in forensic analysis exactly as described in the specification as originally filed, without the need for **any** further research. Even if the

use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as described in the instant specification to be of use to forensic science. As stated above, using the polymorphic markers as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added).

Furthermore, Applicants point out that the standard for meeting the requirements of 35 U.S.C. § 101 is not whether further experimentation is required to practice the claimed invention, but whether **undue** experimentation would be required to practice the claimed invention. The widespread use of polymorphisms such as those described by Applicants in forensic analysis every day **strongly** argues against such a use requiring "undue experimentation". In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. Applicants respectfully point out that all that is required to support this assertion of utility is for the skilled artisan to believe that the presently described polymorphic

markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Applicants **every day** provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Applicants in the same fashion. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Absent such evidence from the Examiner, as the skilled artisan would readily understand that the present polymorphic markers have utility in forensic analysis, the present claims have a substantial and well established utility, and therefore clearly meet the requirements of 35 U.S.C. § 101.

Applicants additionally point out that the present invention has the utility of tracking expression of the presently claimed sequence. The specification details, at least at page 6, lines 4-6, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776 (**Exhibits E-J**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). As the present sequences are specific markers of human chromosome 9 (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial

utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, *Science* **291**:1304, 2001; **Exhibit K**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, *Science* **291**:1153, 2001; **Exhibit L**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Examiner also discounts this asserted utility, again stating that this utility is applicable to "any nucleic acid" (Action at page 3). This argument is flawed in at number of respects. First, Applicants respectfully point out that not just "any nucleic acid" can be used to assess the level of gene expression, but rather only those sequences that are expressed. Second, Applicants point out that the present sequence, which has been biologically validated to be expressed, has a much greater utility than sequences that are merely predicted to be expressed based on bioinformatic analysis. Third, the Examiner again appears to be confusing the requirements of a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that a small number of other nucleotide sequences are expressed and thus able to assess the level of gene expression does not mean that the use of Applicants' sequence to assess the level of gene expression is not a specific utility (*Carl Zeiss*, *supra*; "[A]n invention need not be the best or only way to accomplish a certain result"). The holding in *Carl Zeiss*, and particularly the quote provided above, clearly states that an invention does not need to be the only way to accomplish a certain result. Applicants reiterate that the question of whether or not other nucleic acid sequences can be used to assess the level of gene expression using DNA chips is completely irrelevant to the present utility inquiry. The **only** relevant question in regard to meeting the standards of 35 U.S.C. § 101 is whether **every** nucleic acid can be so used - and the clear answer to this question is an emphatic **no**. Importantly, the holding in *Carl Zeiss* is mandatory legal authority that essentially controls the outcome of the present case. This case, and particularly the cited quote, directly rebuts the Examiner's argument. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

As yet a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 3, lines 2-4, the present nucleotide sequences have a specific utility in "identification of protein coding sequences" and "mapping a unique gene to a particular chromosome". As described in the specification as originally filed at page 3, lines 5-6, the gene encoding the presently claimed sequences is present on "human chromosome 9, see GENBANK accession no. AL354982". In fact, alignment of SEQ ID NOS:3 and 5 with GenBank accession numbers AL158158, AL592463 and AL354982 (three overlapping genomic clones from human chromosome 9) shows that the human gene corresponding to SEQ ID NOS:3 and 5 is dispersed on 48 or 33 exons, respectively, of human chromosome 9 (alignments and first pages of the GenBank reports are presented in **Exhibit M**). Clearly, the claimed polynucleotides provides exquisite specificity in localizing the specific region of human chromosome 9 that contains the gene corresponding to the claimed polynucleotides, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra*, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions this utility, again stating that this utility is applicable to "any nucleic acid" (Action at page 3). First, Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). As described in the specification as originally filed at page 3, lines 7-9, the claimed sequences "identify biologically verified exon splice junctions, as opposed to splice junctions that may have been bioinformatically predicted from genomic sequence alone". The

specification also details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification at page 11, lines 14-19). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

Second, the Examiner again appears to be confusing the requirements of a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. The fact that a small number of other nucleotide sequences are expressed in this specific region of human chromosome 9 and thus able to determine the genomic structure of this particular locus does not mean that this use of Applicants' sequence is not a specific utility (*Carl Zeiss*, *supra*; "[A]n invention need not be the best or only way to accomplish a certain result"). Once again, the holding in *Carl Zeiss*, and particularly the quote provided above, clearly states that an invention does not need to be the only way to accomplish a certain result. Applicants reiterate that the question of whether or not other nucleic acid sequences can be used to determine the genomic structure of this locus is completely irrelevant to the present utility inquiry. The **only** relevant question in regard to meeting the standards of 35 U.S.C. § 101 is whether **every** nucleic acid can be so used - and the clear answer to this question is an emphatic **no**. Once again, the holding in *Carl Zeiss* is mandatory legal authority that essentially controls the outcome of the present case. This case, and particularly the cited quote, directly rebuts the Examiner's argument. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme

Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides; **Exhibits N-P**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples; **Exhibit Q**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1, 2 and 4-12 under 35 U.S.C. § 101 has been overcome, and request that the

rejection be withdrawn.

IV. Rejection of Claims 1, 2 and 4-12 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1, 2 and 4-12 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

First, while Applicants in no way agree with the Examiner's position that one skilled in the art would not know how to use the invention as set forth in claim 2, since claim 2 has been cancelled entirely without prejudice and without disclaimer solely in order to more rapidly progress the present case to allowance, the present rejection of claim 2 under 35 U.S.C. § 112, first paragraph is rendered moot. The remainder of this section will therefore focus on claims 1 and 4-12.

Applicants submit that as claims 1 and 4-12 have been shown to have "a specific, substantial, and credible utility", as detailed in section III above, the present rejection of claims 1 and 4-12 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1, 2 and 4-12 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term "highly stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of highly stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance, claim 2 has been cancelled without prejudice and without disclaimer, rendering the present rejection moot.

As the rejection of claim 2 under 35 U.S.C. § 112, second paragraph, has been overcome, Applicants respectfully request withdrawal of this rejection.

VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Turner have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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